

REMARKS

Entry of this Amendment is proper under 37 C.F.R. § 1.116, because the Amendment places the application in condition for allowance for the reasons discussed herein; does not raise any new issue requiring further search and/or consideration, because the amendments amplify issues previously discussed throughout prosecution; and places the application in better form for an appeal should an appeal be necessary.

As correctly stated in the Office Action Summary, claims 1-21, 23, 31, 33-46, 48-86, 88-99, 101-108, and 110-137 are currently pending. Claims 2-21, 26-31, 33-46, 48-75, 77-86, 88-99, 101-108, 110-125, and 127-137 stand withdrawn as drawn to a nonelected invention.

Claims 1, 23-25 and 126 are amended herein. New claims 138-146 are added. Basis for the amendments to the claims and new claims may be found throughout the specification and claims as-filed, especially at page 7, line 24 to page 8, line 6; and page 8, lines 17-37.

Claims 2-21, 26-125 and 127-137 are canceled herein as directed to non-elected subject matter, without prejudice or disclaimer thereto. Applicants reserve the right to file at least one continuation or divisional application directed to any subject matter canceled by way of the present Amendment.

Objection

The specification stands objected to, as the Office Action states that the phrase "incorporated by reference", as referring to International Application No. PCT/SE99/00544 and the Swedish Patent Application Nos. 9801164-6 and 9900319-6 on page 1 of the specification was not part of the specification as originally filed. Applicants submit that this subject matter, with regard to "incorporation by reference" is not "new matter. However, without acquiescing in the objection, the specification is amended to the term "incorporation by reference". Thus, Applicants request that this objection be withdrawn.

Rejection Under 35 U.S.C. § 112, Second Paragraph

Claims 1, 24-25 and 126 stand rejected under 35 U.S.C. 112, second paragraph, as purportedly indefinite. Specifically, the Office Action states that the term "same biological activity" is unclear.

Applicants have amended the claims by way of the present Amendment such that the phrase is no longer recited. Thus, this rejection is obviated.

Claims 24-25 stand rejected for reciting "from about amino acid No.", as it is purportedly unclear how many amino acids constitute "about". Claims 24-25 are amended herein to remove the term "about". Thus, this rejection is obviated.

In light of the above remarks and amendments to the claims, Applicants request that the rejections under 35 U.S.C. § 112, second paragraph, be withdrawn.

Rejections Under 35 U.S.C. § 112, First Paragraph**Enablement**

Claims 1, 23-25, 76, and 126 stand rejected under 35 U.S.C. § 112, first paragraph, as purportedly failing to satisfy the enablement requirement. Specifically, the Office Action states that the specification does not provide sufficient guidance as to which subsequences of SEQ ID NO:2 would share the same biological activity, and which amino acid sequences are essential.

As stated in *In re Wands* (858 F.2d 731, 737, 8 U.S.P.Q. 2d 1400, 1404 (Fed. Cir. 1988)) the factors to consider when evaluating the need (or absence of need) for "undue experimentation" are the following: quantity of experimentation necessary, amount of direction or guidance presented, presence or absence of working examples, nature of the invention, state of the prior art, relative skill of those in that art, predictability or unpredictability of the art, and breadth of the claims. Applicants submit that the claims, as set forth herein, meet the requirements for enablement.

As set forth herein, the claims no longer recite "biological activity". In addition, claims 1, 23-25, 76, and 126 are amended to recite specific subunits and specific fragments thereof of the integrin subunit. Specifically, the claims as amended and added herein recite the recombinant or isolated collagen binding integrin subunit comprising SEQ ID NO:2 or SEQ ID NO:4 or fragments thereof, wherein the fragments are amino acid 952 to amino acid 986 of SEQ ID NO:2, amino acid 140 to amino acid 337 of SEQ ID NO:2 and SEQ ID NO:7 as appropriate. Thus, no undue experimentation is required for the skilled artisan to determine which sequences may be used in the present invention.

To address comments by the Examiner in the outstanding Office Action, Applicants refer to page 5, last paragraph of the Office Action, where the Examiner refers to $\alpha 1\beta 1$ integrin receptors. Applicants note that this was a typographical error. Rather, Applicants meant to recite $\alpha 10\beta 1$, and the provided data is for the use of antibodies to the $\alpha 10\beta 1$ integrin receptor. The Examiner further states that it is unclear what types of cells were used with the present invention. Applicants note that it is clearly primary human chondrocytes which are used in Appendix B, as referenced under the figure showing the FACS analysis identifying primary human chondrocytes. Finally, on page 5, last paragraph of the Office Action, the Examiner states that Applicants are attempting to show that $\alpha 10$ is only present in chondrocytes in cartilage. This is not the case. Applicants set forth that chondrocytes, as the only cells of cartilage, express $\alpha 10$. Thus, $\alpha 10$ may be readily used to detect the presence of cartilage.

In summary, the claims are amended to recite specific sequences such no undue experimentation is required for the skilled artisan to determine which sequences may be used in the present invention. Applicants submit that in light of the amendments made herein and the specific sequences recited in the specification, the skilled artisan would be able to successfully practice the present invention.

Written Description

Claims 1, 23-25, 76 and 126 stand rejected under 35 U.S.C. 112, first paragraph, as purportedly containing subject matter which was not described in the

specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Specifically, the Office Action states that Applicants are not in possession of:

- any recombinant or isolated collagen binding integrin subunit $\alpha 10$ comprising essentially the amino acid sequence shown in SEQ ID NO:2, or homologues or fragments thereof having essentially the same biological activity in claim 1;
- any fragment of the integrin subunit $\alpha 10$, wherein the fragment is the amino acid sequence from about amino acid No. 952 to about amino acid No. 986 of SEQ ID NO: 2 in claim 24;
- any fragment of the integrin subunit $\alpha 10$, wherein the fragment is the amino acid sequence from about amino acid No. 140 to about amino acid No. 337 of SEQ ID NO: 2 in claim 25; and
- vaccine comprising the subunit $\alpha 10$, or a homologue or fragment of said integrin or subunit $\alpha 10$, wherein the fragment is selected from the group consisting of the cytoplasmic domain, the I-domain and the spliced domain in claim 76 or the integrin subunit $\alpha 10$ of SEQ ID NO:2, wherein the integrin subunit $\alpha 10$ is a marker or target in transplantation of cartilage or chondrocytes.

Applicants submit that in light of the amendment made herein, the above comments no longer apply to the present claims. As noted above, the claims presented herein recite the recombinant or isolated collagen binding integrin subunit comprising SEQ ID NO:4 or fragments thereof, wherein the fragments are amino acid 952 to amino acid 986 of SEQ ID NO:2, amino acid 140 to amino acid 337 of SEQ ID NO:2 and SEQ ID NO:7 the inventors, at the time the application was filed, had possession of the claimed invention as set forth herein. Finally, the claims directed to a vaccine are canceled herein.

In light of the above, Applicants request that the rejections under 35 U.S.C. § 112, first paragraph, be withdrawn.

Rejections Under 35 U.S.C. § 102(b)

Claims 1 and 126 stand rejected under 35 U.S.C. § 102(b) as purportedly anticipated by Takada. Takada purportedly teaches a human $\alpha 3$ subunit, an integrin receptor for collagen, as well as nine amino acid sequence of metal binding domains general structure (DX(DbN)X(D/N)GXXD)) fragment. The Office Action states that “a marker or target in transplantation of cartilage or chondrocytes” is an inherent property.

Applicants submit that Takada fails to recite every element of the presently claimed invention, as amended herein. To anticipate a claim, a single prior art reference must teach each and every element of the claimed invention. See M.P.E.P. § 2131; *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 U.S.P.Q.2d 1051, 1053 (Fed. Cir. 1987); *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1379, 231 U.S.P.Q. 81, 90 (Fed. Cir. 1986).

As amended herein, claim 1 is directed to a recombinant or isolated collagen binding integrin subunit $\alpha 10$ consisting of SEQ ID NO: 2 or fragments thereof, wherein the fragments are selected from the group consisting of amino acid 952 to amino acid 986 of SEQ ID NO: 2, amino acid 140 to amino acid 337 of SEQ ID NO: 2, and SEQ ID NO: 7. Claim 126 is now directed to the integrin subunit $\alpha 10$ of claim 1, wherein the integrin subunit $\alpha 10$ is a polypeptide attached to a detectable moiety for detecting presence of transplanted cartilage or transplanted chondrocyte cells expressing said polypeptide in a subject transplanted with said cartilage or chondrocyte cells. Takeda fails to recite each element of the claims invention, as Takeda is merely directed to a human $\alpha 3$ subunit, in contrast to the $\alpha 10$ subunit of the present invention, as well as sequences of the general structure

(DX(DbN)X(D/N)GXXD)) fragment. Thus, Takeda does not recite the sequences recited in the present claims as amended herein.

Finally, the outstanding Office Action states that the claim element "marker or target in transplantation of cartilage or chondrocytes" is an inherent property of the claims. The fact that a certain result or characteristic may occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic. *In re Rijckaert*, 9 F.3d 1531, 1534, 28 USPQ2d 1955, 1957 (Fed. Cir. 1993); *In re Oelrich*, 666 F.2d 578, 581-82, 212 USPQ 323, 326 (CCPA 1981). In relying upon the theory of inherency, the examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art. *Ex parte Levy*, 17 USPQ2d 1461, 1464 (Bd. Pat. App. & Inter. 1990).

As amended herein, the claims recite specific sequences for use with the claimed invention, which are not identical to those recited in Takada. The Office Action has not met the burden of providing a basis in fact and/or technical reasoning showing that the purportedly inherent property of being a marker or target in transplantation of cartilage or chondrocytes flows from the Takada reference, especially as Takada does not recite the same sequences as the presently claimed invention.

In light of the above, Applicants request that the rejection under 35 U.S.C. § 102 be withdrawn.

CONCLUSION


From the foregoing, further and favorable action in the form of a Notice of Allowance is respectfully requested and such action is earnestly solicited.

In the event that there are any questions concerning this amendment or the application in general, the Examiner is respectfully requested to telephone the undersigned so that prosecution of the application may be expedited. The Director is hereby authorized to charge any appropriate fees under 37 C.F.R. §§ 1.16, 1.17, 1.20(d) and 1.21 that may be required to maintain pendency, including the fee for the Notice of Appeal, should these papers become separated, to Deposit Account No. 02-4800.

Respectfully submitted,

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